

# Clinicopathological Features of Esophageal Cancer Simultaneously Associated With Gastric Cancer

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**Background and Objectives:** We usually use the stomach for esophageal substitution in the surgical treatment of esophageal cancer, although it is often associated with gastric cancer. In order to improve the likelihood of safe and curative surgery of esophageal cancer, we investigated the clinicopathological characteristics of synchronous esophageal and gastric cancer.

**Methods:** Among 288 patients with primary esophageal cancer who had undergone esophageal resection, this cancer was associated with gastric cancer in 11 cases, and 1,416 gastric cancer patients operated on during the same period, were analyzed. The clinicopathological characteristics and surgical procedures of the 11 patients were compared with those of the other esophageal cancer patients and with those with the gastric cancer only.

**Results:** There were significant differences between the synchronous double cancer and the gastric cancer only in sex ( $P < 0.01$ ) and location of the gastric cancer ( $P < 0.05$ ). All of the patients with the synchronous double cancer were men, and the incidence of patients with cardiac cancer was high.

**Conclusions:** Our findings suggest that, in cases of synchronous esophageal and gastric cancer, an adequate surgical procedure must be chosen in terms of the stage, location, and operative burden.

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**KEY WORDS:** synchronous double cancer; esophagectomy; gastrectomy; reconstruction

## INTRODUCTION

Esophageal cancer is primarily known to be associated with head and neck and respiratory cancer [1,2], but the incidence of its association with gastric cancer is also high, especially in Japan [3–5]. As for the surgical treatment of concurrent esophageal cancer, the procedures are usually independent of each other; whereas in cases associated with gastric cancer, we have to choose either the colon or the remaining stomach for reconstruction, instead of the esophagus. It is therefore important to determine whether gastric cancer is present or not, and also to identify the location and the stage of the gastric cancer. In the current study, we retrospectively investigated the characteristics of cases of esophageal cancer associated

with gastric cancer, paying special attention to the location and the stage of the gastric cancer.

## PATIENTS AND METHODS

Between 1970 and 1996, 288 patients with primary esophageal cancer underwent esophageal resection in our department. Among them, 17 patients (5.9%) had concurrent cancer in another organ. The associated organs were the stomach in 11 cases (3.8%), the pharynx and

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TABLE I. Clinicopathological Features of the Esophageal and Gastric Cancers

Patient no.	Age/Sex	Esophageal cancer		Gastric cancer			Organ used for reconstruction
		Location	TNM	Location	TNM	Resection of gastric cancer	
1	75/M	Lower	T2N0M0	Lower	T1N0M0	Distal gastrectomy	Jejunum
2	70/M	Upper	T4N1M0	Upper	T3N0M0	Wedge resection	Stomach
3	74/M	Middle	T3N1M0	Upper	T1N0M0	Endoscopic resection	Stomach
4	43/M	Middle	T2N0M0	Upper	T3N0M0	Cardiac gastrectomy	Colon
5	51/M	Middle	T1N0M0	Upper	T3N0M0	Cardiac gastrectomy	Colon
6	55/M	Middle	T1N0M0	Middle	T1N0M0	Total gastrectomy	Colon
7	71/M	Middle	T3N1M0	Lower	T1N0M0	Total gastrectomy	Colon
8	52/M	Lower	T1N0M0	Middle	T3N2M0	Total gastrectomy	Colon
9	66/M	Lower	T1N0M0	Upper	T1N0M0	Total gastrectomy	Colon
10	50/M	Middle	T1N1M0	Middle	T3N0M0	Total gastrectomy	Colon
11	57/M	Upper	T1N1M0	Lower	T3N1M0	Wedge resection	Stomach
				Upper	T2N2M0		

larynx in two cases each, and the uterus and thyroid gland in one case each. Fifteen patients (5.2%) had metachronous cancer in the esophagus and another organ, and in two of these cases the gastric cancers occurred 3 and 14 years, respectively, after esophageal resection. A comparative analysis was made of 1,416 patients with gastric cancer, who were surgically resected during the same period and histologically examined. The clinicopathological characteristics and surgical procedures for the 11 concurrent esophageal and gastric cancer patients were compared with those for the other esophageal cancer and the gastric cancer-only patients, with particular attention to location and stage determined according to the TNM classification. Statistical analysis was performed using the chi-square test, Student's *t*-test for independence means, and Fisher's exact test. All tests of significance were two-tailed, and a *P*-value of <0.05 was considered statistically significant.

## RESULTS

The 11 patients with concurrent esophageal and gastric cancer were all men, with an average age of  $60.4 \pm 11.2$  years (range: 43–75). Two of the esophageal cancers were located in the upper, six in the middle, and three in the lower thoracic esophagus. Of the 11 patients who underwent esophagectomy and reconstructive procedure, the stomach was used as an esophageal substitute in three, the colon in seven, and the jejunum in one case. Two of the six cases with gastric lesions located in the upper third had the affected gastric wall with the lymph nodes resected, and one had the gastric tumor limited to the mucosa endoscopically excised. In these three cases, the esophagus was reconstructed by using the remaining stomach (Table I). Comparison of the clinicopathological factors for esophageal cancers with gastric cancer and those without gastric cancer showed no differences in age, sex, location, lymph node metastasis, or histology

(Table II). The total of 13 gastric lesions is accounted for by two of the 11 concurrent cases who had two gastric cancer lesions. Five of these 13 lesions (38.5%) were early gastric cancers, compared with 441 of 1,416 lesions (31.3%) in the gastric cancer-only group. With regard to location of the gastric lesion, six of the 13 gastric lesions (46.2%) were located in the upper third, three (23.0%) in the middle third, and four (30.8%) in the lower third—so that the incidence of upper third lesions is significantly high, as compared with that of the gastric cancer-only (*P* < 0.05). Three of the 11 concurrent cases (27.3%) had lymph node metastasis, compared with the incidence of lymph node metastasis for the gastric cancer-only of 55.2% (781/1,416). Histologically, 10 of the 13 lesions were intestinal-type, and three diffuse-type adenocarcinomas (Table III).

## DISCUSSION

Squamous cell carcinoma of the esophagus is frequently associated synchronously with other primary cancers, especially head and neck cancers [1,2]. The incidence of association with gastric adenocarcinoma is not so high in western countries [3,4], but has sometimes been reported in Japan [5]. According to a nationwide survey by the Japanese Committee of Esophageal Disease in 1980, the synchronous double cancers with esophageal cancer accounted for 251 out of 11,732 resected cases—and 186 cases (1.6%) of these were associated with gastric cancer [6]. Also, a multicentric study of 22,163 cases of gastric cancer, operated on and followed up for 10 years in Japan, estimated the frequency of this association at 0.2% of all gastric cancers [7].

The present study documents that a comparison of clinicopathological items shows no difference between the synchronous double cancer and the other esophageal cancer patients, whereas between them and the patients with gastric cancer only, there were significant differ-

**TABLE II. Comparison of Clinicopathological Factors Between Gastric Cancer Patients With and Without Esophageal Cancer**

Factors	With or without esophageal cancer		<i>P</i> -value <sup>a</sup>
	With (n = 11, 13 lesions)	Without (n = 1416)	
Mean age	60.4 ± 11.2	60.1 ± 12.0	<i>P</i> = 0.8334 (NS)
Sex (M:F)	11:0	914:502	<i>P</i> = 0.0083
Location <sup>b</sup>			
Upper	6 (1)	300 (56)	<i>P</i> = 0.0402
Middle	3 (2)	433 (185)	
Lower	4 (2)	549 (188)	
Others <sup>c</sup>	0	134 (12)	
Lymph node metastasis from gastric cancer			
Positive	3	781	<i>P</i> = 0.0604 (NS)
Negative	8	634	
Unknown	0	1	
Histology			
Differentiated adenocarcinoma	10	714	<i>P</i> = 0.0534 (NS)
Undifferentiated adenocarcinoma	3	690	
Unknown	0	12	

<sup>a</sup>NS, not significant.<sup>b</sup>Numbers in parentheses are early cancers.<sup>c</sup>Tumor is situated in two or three areas.**TABLE III. Comparison of Clinicopathological Factors Between Esophageal Cancer Patients With and Without Gastric Cancer**

Factors	With or without gastric cancer		<i>P</i> -value <sup>b</sup>
	With (n = 11)	Without (n = 275) <sup>a</sup>	
Mean age	60.4 ± 11.2	61.2 ± 12.4	0.8334 (NS)
Sex (M:F)	11:0	213:62	0.0644 (NS)
Location			
Cervical	0	22	0.4569 (NS)
Upper thoracic	2	37	
Middle thoracic	6	168	
Lower thoracic	3	48	
Lymph node metastasis from esophageal cancer			
Positive	5	156	0.2556 (NS)
Negative	6	104	
Unknown	0	15	
Histology <sup>c</sup>			
Well differentiated SCC	6	74	0.0538 (NS)
Moderately differentiated SCC	2	69	
Poorly differentiated SCC	0	87	
SCC <sup>d</sup>	3	28	
Unknown <sup>e</sup>	0	17	

<sup>a</sup>This number excludes two patients with esophageal cancer following resection of gastric cancer.<sup>b</sup>NS, not significant.<sup>c</sup>Well, moderately, or poorly differentiated squamous cell carcinoma (SCC).<sup>d</sup>Degree of differentiation of SCC is unknown because of radiation.<sup>e</sup>No viable cancer cells are seen because of marked effect of radiation.

ences in sex and location (*P* = 0.0083 and *P* = 0.0402, respectively). Concerning sex, it is reported that for synchronous double cancers with esophageal cancer, the rate of male to female is 9:1 [6], and for gastric cancer patients 2:1 in Japan [7]. Therefore, it can be assumed that concurrent esophageal and gastric cancer patients are almost exclusively male. In addition, the sex ratio varies

according to the site of gastric cancer, with cancer of the cardia affecting men four times as frequently as it does women. The sex ratio for cancer of the pylorus is only 1.5 [8].

The proportion of patients with cancer of the cardia is generally lower than that of patients with cancer of the corpus and antrum, although in our study the proportion

of patients with gastric cancer in the upper third of the stomach associated with esophageal cancer is significantly higher ( $P = 0.0402$ ) than that of the patients with gastric cancer only. Since in the surgical treatment of esophageal cancer the stomach is usually used for esophageal substitution, it is important to determine whether gastric cancer is present, and also to identify its locations. If the distribution of the location of gastric cancer associated with esophageal cancer is almost the same as that of gastric cancer-only, there is a possibility that gastric lesions located in the corpus and antrum will be overlooked—even though in cases of concurrent esophageal and gastric cancer, a high incidence of proximal gastric cancer can be expected.

Kato et al. [5] reported that gastric carcinoma associated with esophageal carcinoma tends to occur in the proximal part of the stomach more frequently than does gastric carcinoma-only. The reported increase in proximal gastric cancer cases might therefore correspond to the increase in the number of patients with esophageal cancer [9]. In western countries, an increase in the proportion of patients with cardia carcinoma was noted in recent years. It is reported that the proportion of patients with intestinal-type carcinoma has decreased over the same period, while the proportion of patients with diffuse-type carcinoma has increased [10]. It is therefore thought that carcinogenesis of both esophageal cancer and gastric cancer in the cardia is affected by common carcinogenic substances. Concerning the epidemiology: Alcohol and smoking are very common epidemiologic factors associated with esophagus, head and neck cancers [1,2]. The fact that smoking and alcohol have been particularly associated with proximal tumors led Hirayama to hypothesize that the carcinogenic effect of smoking may affect the cardia region more than other sites [11]. In terms of nutrition, a nationwide survey of the Japanese Ministry of Health and Welfare established a positive relationship between salty foods (like pickled vegetables and dried fish) and both esophageal and gastric cancer [12]. The contribution of nitrosamines to the pathogenesis of gastric cancer has also been established both experimentally and clinically. In rats, some nitrosamines selectively produced tumors of the forestomach and also acted as a more potent esophageal carcinogen; whereas the glandular portions of the stomach proved highly resistant to these compounds [9].

Surgical procedures such as total esophagectomy and total gastrectomy should be performed only when there is a high probability of a curative operation, because of the frequent occurrence of multicentric cancer lesions of the stomach and the complicating presence of lymph node metastases. Since an invasive operation is not recommended for elderly patients or patients suffering from complications and general malnutrition, other treatments

should be considered, such as radiotherapy for esophageal cancer after gastrectomy and chemotherapy for both esophageal and gastric cancers. However, if the gastric cancer is located in the cardia, there is a possibility of less radical surgery by means of partial or wedge resection of the gastric tumor together with the lymph nodes and reconstruction of the esophagus by utilizing the remaining stomach. We also used the stomach combined with a wedge resection for two of the six concurrent cancer patients with gastric cancer located in the cardia, and with endoscopic resection for one. The appropriate surgical procedures must be selected, taking into account the location and stage of gastric cancer, and also the stress caused by invasive surgery; esophageal cancer represents the prognostic variable in most patients with concurrent esophageal and gastric cancer.

## CONCLUSIONS

In the case of patients with esophageal cancer, the high incidence of concurrent gastric cancer makes it essential to examine the stomach very carefully, especially the upper third. Furthermore, if gastric cancer is present, its location and stage must be determined. The remainder of the stomach can then be used as an esophageal substitute depending on the curability of the esophageal cancer.

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